REMARKS

1. The Office Action mentioned that "the specification does not describe a cell culture device for recovering mesenchymal stem cells from a mixture of cells in which the pore size ranges from 0.4 to 20 microns. Thus, the newly added limitation to claim 1 constitutes new matter." The newly added limitation to claim 1 by narrowing the pore size is, of course, within the original range, 04 to 40 microns. In other words, the new limitation is within the original scope, which shall not constitute a new matter.

As MPEP 2163.06, Relationship of Written Description Requirement to New Matter, states, "information contained in any one of the specification, claims or drawings of the application as filed may be added to any other part of the application without introducing new matter."

In Heymes v. Takaya, 6 U.S.P.Q.2d 1448 (Bd. Pat. App. & Int. 1988), aff'd, 10 U.S.P.Q.2d 1473 (Fed. Cir. 1989), the Board noted that it is not necessary that the claimed subject matter be described in ipsis verbis to satisfy the written description requirement of 35 U.S.C. §112. Accordingly, in view of the Heymes holding, the written description requirement does not require a description of subject matter in "ipsis verbis," nor does it require a specific example. Id. at 1452.

In In re Wertheim, 541 F.2d at 263, 191 U.S.P.Q. at 97, the CCPA made it clear that "[b]roadly articulated rules are particularly inappropriate" in applying the description requirement to narrowed claims involving ranges. In that case, the CCPA held that the PTO failed to establish a prima facie case of noncompliance with the description requirement even though there was lack of literal support. The PTO

presented no evidence that one skilled in the art would not view the narrower range as within Wertheim's invention

Furthermore, one of the most famous examples is the case of Hilton Davis Chemical Co. v. Waner-Jenkinson Company, Inc, in which the range of the pH value was also narrowed. Neither the judges of Supreme Court nor the judges of CAFC (en banc) mentioned the "new matter" issue. Therefore, the new limitation within the original scope shall not constitute a new matter.

2. The Office Action also mentioned that "the cell mixture can comprise any type of cell, particularly since the specification discloses that the cell mixture can be obtained from fractioned tissue, unfractioned tissue and a body fluid. Many types of cells, other than MSC, have the ability to adhere to a tissue culture plate and are large in size that they will not pass through the pores."

To clarify the point, the applicants have re-amended claim 1 by adding the "small-sized" limitation, which is supported by the specification of this application as "small-sized haematopoietic cells can pass through the pores in the plate to reach the plate base before adhering." [0029]

Furthermore, claim 5 has been canceled in this amendment. Therefore, the cells are selected from the group consisting of a bone marrow, an embryonic yolk sac, a placenta, an umbilical cord, a fetal, adolescent or adult body fluid, and a fetal, adolescent or adult tissue. Among those cells, the MSC in bone marrow has been reported to "increase in size and express increased level of osteocalcin and alkaline phosphatase." (Long et al. J. Clin. Invest. 1995 Vol. 95 pp. 881-887).

Van Vlasselaser et al. (Blood, 1994 Vol 83 No 3, pp 753-763) also reported that "cells from the FSC^{high} SSC^{high} gate, but not from the other gates, synthesized alkaline phosphatase, collagen, and osteocalcin and formed a mineralized matrix in culture." Colter et al. (PNAS 2000 March Vol 97 No 7 pp 3213-3218) also described that "the FACS analyses carried out here demonstrated that stationary cultures of MSCs contained a major population of large cells here referred to as mMSCs and a minor population of small and agranular cells (RS-1 cells)." It is stated exactly in this application that: "By means of their characteristics of large size (van Vlasselaer P, et al., supra), ease to adhere and their role in supporting haematopoietic stem cells (Huang S., et al., Nature 360:745, 1993), the method of the present invention was developed with the use of a culture device to physically isolate early MSCs. (2002/0045260A1 2 [024]).

Furthermore, US Patent 5,486,359, previously cited by the examiner, also stated that: "In order to obtain subject human mesenchymal stem cells, it is necessary to isolate rare pluripotent mesenchymal stem cells from other cells in the bone marrow or other MSC source. Bone marrow cells may be obtained from iliac crest, femora, tibiae, spine, rib or other medullary spaces. Other sources of human mesenchymal stem cells include embryonic yolk sac, placenta, umbilical cord, fetal and adolescent skin, and blood." (II lines 14~21). The 5,486,359 patent also mentioned that "when cultured, for the selective adherence of only the mesenchymal stem cells to a substrate surface, culturing the specimen-medium mixture, and removing the non-adherent matter from the substrate surface." (II lines 26-29). In addition, Huss et al. also

disclosed the evidence of peripheral blood-derived, plastic-adherent $CD34^{-/low}$ hematopoietic stem cell. (Stem Cells, 2000 Vol 18, pp 252-260).

In sum, the MSC has the characteristics of large size and plastic adherence, which are supported by many published articles as well as patents. Therefore, one skilled in the art can use this application for better results of MSC isolation.

3. Patent Law does not require a perfect device to be granted a patent, as the Law states "whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title."

The Office Action stated that "it is unlikely that the cell culture device described will only allow MSCs to adhere to the plate and allow all cells but MSC to pass through the pores." However, this application combining the characteristics of large size and plastic adherence can result in a "novel, simple, effective, and economic method of isolating MSCs." [0023]. In other words, this application is not perfect, but it does help in MSC recovery, as the application stated: "In one preferred embodiment, cell populations having greater than 98% of human MSCs can be obtained in accordance with the method of the invention, and such isolated MSCs can proliferate without differentiation and reach confluence even after 12 passages." [0011].

4. Narrowing a claim within the original scope shall not constitute a new matter. Furthermore, the MSC has the characteristics of large size and plastic adherence, which are supported by many published articles as well

as patents. This application is the first one to combine the two features together and to improve the isolation of MSCs. Accordingly, this application now should be placed in condition of allowance. An early Notice to this effect is respectfully requested.

Respectfully submitted:

By: Shih-Chieh Hung

Shih-Chieh Hung
886-2-28757557 ext 118 (voice)
886-2-28265164 (fax)
hungsc@vghtpe.gov.tw (email)
No 201 Shih-Pai Rd Section II,
Taipei-Veterans General Hospital,
Taipei, Taiwan, R. O. C.